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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/549,848 | 04/14/2000 | Michael Lassner | 17133/02/US | 9155 |

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|---|---|
| COLLINS, CYNTHIA E | |
| ART UNIT | PAPER NUMBER |
| 1638 | |

DATE MAILED: 06/18/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/549,848 | Applicant(s) LASSNER ET AL. | |
|---|---|---|---|
| | Examiner Cynthia Collins | Art Unit 1638 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *03 April 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *13,18-33,36,39 and 42-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1,13 and 18* is/are allowed.

6)☒ Claim(s) *19-33,36,39 and 42-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

The Amendment filed April 9, 2002, paper no.20, has been entered.

Claims 2, 3, 4, 11, 12, 14, 15, 16, 17, 34, 35, 37, 38, 40 and 41 have been cancelled.

Claims 1, 13, 18, 24, 36 and 39 have been newly amended.

Claims 42-44 have been newly added.

Claims 1, 13, 18-33, 36, 39 and 42-44 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Specification*

The objection to the disclosure because the text on page 42 refers to the expression of "ATAT2" rather than "ATPT2" is withdrawn in light of the amendment of page 42.

### *Claim Objections*

The objection to claims 35, 38, 40 and 41 for reciting the SEQ ID NOS of nonelected inventions is withdrawn in light of the cancellation of claims 35, 38, 40 and 41.

### *Claim Rejections - 35 USC § 112*

The rejection of claims 1-4, 11-12, 13-18 and 34 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, is withdrawn in light of the cancellation of claims 2, 3, 4, 11, 12, 14, 15, 16, 17 and 34, and the amendment of claims 1, 13 and 18.

Claims 36 and 39 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the office action mailed January 3, 2002.

Applicant's arguments filed April 9, 2002, have been fully considered but they are not persuasive.

Applicant argues that an adequate written description of a genus of nucleic acids may be achieved either by a recitation of a representative number of sequences falling within the scope of the genus, or a recitation of structural features common to the genus members. Applicant argues that the specification discloses seven putative *Arabidopsis* straight-chain class prenyltransferases and five putative *Arabidopsis* aromatic class prenyltransferases, as well as multiple sequences for aromatic prenyltransferases from soy, maize and *Synechococcus*. Applicant argues that a representative number of nucleic acid sequences has been disclosed, and that the specification provides experimental evidence that such sequences encode a functional protein (reply page 6).

Claims 36 and 39 are drawn to isolated nucleic acid molecules encoding a prenyltransferase wherein the prenyltransferase is from corn or from soybean. The specification describes nucleotide sequences putatively encoding five aromatic prenyltransferases from soybean (nonelected SEQ ID NOS 19-23), and six aromatic prenyltransferases from corn (nonelected SEQ ID NOS 25-29 and 31), said sequences having been isolated on the basis of the homology of their encoded polypeptides to the *E. coli* aromatic prenyltransferase ubiA (pages

22-23). None of the soybean or corn nucleotide sequences described in the specification encode a full-length open reading frame (Sequence Listing). The specification does not provide any experimental evidence that any of the soybean or corn nucleotide sequences encode a polypeptide having a prenyltransferase function. The disclosure of five partial nucleotide sequences from soybean that encode truncated polypeptides having homology to the *E. coli* aromatic prenyltransferase ubiA does not constitute a representative number of nucleic acid sequences describing the genus of isolated nucleic acid molecules encoding a prenyltransferase from soybean. Likewise, the disclosure of six partial nucleotide sequences from corn that encode truncated polypeptides having homology to the *E. coli* aromatic prenyltransferase ubiA does not constitute a representative number of nucleic acid sequences describing the genus of isolated nucleic acid molecules encoding a prenyltransferase from corn.

The rejection of claims 1-4, 11-13, 14-18, 34-35, 37-38, and 40-41, under 35 U.S.C. 112, first paragraph, for scope of enablement, is withdrawn in light of the cancellation of claims 2-4, 11-12, 14-17, 34-35, 37-38, and 40-41, and in light of the amendment of claims 1, 13 and 18.

Claims 19-33, 36 and 39 remain rejected, and claims 42-44 are rejected, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of increasing alpha, gamma, delta, and total tocopherol content in *Arabidopsis* seeds by transforming *Arabidopsis* with SEQ ID NO:1, and while being enabling for a method of increasing the level of alpha tocopherol content in the *Synechocystis* knockout mutant slr1736 by transforming slr1736 with SEQ ID NO:1, does not reasonably provide enablement for other

methods using other isolated nucleic acids encoding other prenyltransferases, for the reasons of record set forth in the office action mailed January 3, 2002.

Applicant's arguments filed April 9, 2002, have been fully considered but they are not persuasive.

Applicant argues that the specification discloses methods for making and using the claimed invention, a variety of sequences that can be used to transform host cells, as well as examples of cells and plants that have been transformed with the sequences. Transgenic plants having seeds with increased tocopherol are also disclosed. Applicant argues that the Examiner has not met the evidentiary burden to impose an enablement rejection because a specification that discloses how to use a claimed invention must be taken as in compliance with35 USC 112 unless there is reason to doubt the objective truth of the statements therein. Applicant argues that the Examiner has provided neither specific evidence to support the rejection, or any explanation of why the specification fails to enable a nucleic acid molecule encoding a prenyltransferase (reply page 7). Applicant disagrees that undue experimentation would be required to practice the claimed invention, and asserts that the Examiner fails to acknowledge the teachings set forth in the specification, which discloses the structure of several prenyltransferase nucleic acid sequences that can be used in the various embodiments of the claimed invention. Applicant points to the disclosure of seven putative *Arabidopsis* straight chain prenyltransferase nucleic acid sequences, five putative *Arabidopsis* aromatic prenyltransferase nucleic acid sequences, as well as the aromatic prenyltransferase sequences from soybean, maize and *Synechocystis*. Applicant argues that the specification discloses how to select genes, construct vectors, and transform plants, as well as how to confirm increased tocopherol levels. Applicant asserts that

the Examiner has not indicated how either of the cited references of Shewmaker et al. or Burkhardt et al. suggest that such work would be undue experimentation (reply pages 8-9).

The Examiner does acknowledge the teachings set forth in the specification, but does not agree that the disclosure enables the scope of the claimed invention. As discussed *supra*, the nonelected nucleic acid sequences putatively encoding aromatic prenyltranferases from soybean and maize do not encode a full-length open reading frame, and the specification does not provide any experimental evidence that these sequences encode a polypeptide having a prenyltransferase function. Although two of the seven putative *Arabidopsis* straight chain prenyltransferase nucleic acid sequences and three of the five putative *Arabidopsis* aromatic prenyltransferase nucleic acid sequences encode a complete open reading frame, the specification only provides experimental evidence that one of these sequences encodes a polypeptide having a prenyltransferase function, the elected nucleic acid sequence of SEQ ID NO:1. Additionally, although the specification provides experimental evidence that two of the nonelected putative *Synechocystis* aromatic prenyltransferase nucleic acid sequences encode a functional protein (slr1736 and slr1737 knockouts), the specification does not disclose the effect of expressing a *Synechocystis* aromatic prenyltransferase nucleic acid sequence in a host cell or plant.

Furthermore, The claims are not drawn to methods of selecting genes, constructing vectors, transforming plants, or confirming increased tocopherol levels. The claims are drawn to isolated nucleic acids encoding prenyltransferases, and methods of using those isolated nucleic acids to alter tocopherol content in a host cell, produce a tocopherol compound in a host cell, and increase biosynthetic flux in a host cell toward tocopherol production. The specification does not provide sufficient guidance for one skilled in the art to determine, without undue

experimentation, which isolated nucleic acid encoding prenyltransferase could be used to alter tocopherol content in a host cell, produce a tocopherol compound in a host cell, and increase biosynthetic flux in a host cell toward tocopherol production, because the specification discloses only a single isolated nucleic acid encoding prenyltransferase that has this effect.

The cited references of Shewmaker et al. or Burkhardt et al. demonstrate unpredictability in that they teach that the expression of a heterologous nucleic acid encoding a particular biosynthetic enzymatic activity (in the case of the cited references phytoene synthase) in a transgenic plant may have different effects depending on the species of plant transformed and the source of the heterologous nucleic acid expressed. The instant claims are drawn to nucleic acids encoding a particular biosynthetic enzymatic activity, and their use in heterologous as well as homologous cell types. Because the effect of expressing a heterologous nucleic acid encoding a particular biosynthetic enzymatic activity in a host cell or organism is unpredictable, there is reason to doubt the objective truth of the statements that the nucleic acid sequences disclosed in the instant application will function to alter tocopherol content in a host cell, produce a tocopherol compound in a host cell, and increase biosynthetic flux in a host cell toward tocopherol production.

Claim 19 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "alteration", for the reasons of record set forth in the office action mailed January 3, 2002.

Applicant's arguments filed April 9, 2002, have been fully considered but they are not persuasive.

Applicant argues that one skilled in the art would be able to ascertain the metes and bounds of "alteration" based on the disclosure. Applicant points to page 5, lines 14-15 of the specification, which states that the invention provides compositions and methods "for altering (for example, increasing and decreasing) the tocopherol levels and/or modulating their ratios in host cells". Applicant asserts that one skilled in the art would recognize "alteration" as reflecting any change in the total or relative amounts of tocopherol compounds (reply page 9).

The Examiner maintains that Applicant has disclosed methods of using an isolated nucleic acid of SEQ ID NO:1 to increase tocopherol content only (pages 40-41 Example 4D and pages 41-42 Example 5). Applicant has not disclosed methods of decreasing tocopherol levels or methods of modulating tocopherol ratios.

The rejection of claim 24 under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "a tocopherol of interest", is withdrawn in light of the amendment of claim 24 to remove the phrase "of interest".

Claim 29 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "increasing the biosynthetic flux in a host cell toward tocopherol", for the reasons of record set forth in the office action mailed January 3, 2002.

Applicant's arguments filed April 9, 2002, have been fully considered but they are not persuasive.

Applicant disagrees that the claim is indefinite or vague, and point out that the claim should be read in light of the specification. Applicant argues that that the meaning of "increasing the biosynthetic flux in a host cell toward tocopherol" is clear when read in the light of the

specification, which provides examples of increased tocopherol and a description of increases, decreases and modulation of ratios of tocopherol compounds (reply page 10).

The Examiner maintains that the meaning of "increasing the biosynthetic flux in a host cell toward tocopherol" is unclear when read in the light of the specification. Applicant has disclosed methods of using an isolated nucleic acid of SEQ ID NO:1 to increase tocopherol content only (pages 40-41 Example 4D and pages 41-42 Example 5). Applicant has not disclosed the effect of an isolated nucleic acid of SEQ ID NO:1 on any other specific aspect of the tocopherol biosynthetic pathway.

***Claim Rejections - 35 USC § 102***

The rejection of claims 1-4 and 13-15 under 35 U.S.C. 102(b) as being anticipated by Kuntz et al. (1992, The Plant Journal, Vol. 2, No. 1, pages 25-34, Applicant's IDS) is withdrawn in light of the cancellation of claims 2, 3, 4, 14 and 15, and the amendment of claims 1 and 13.

Claims 19-20 remain rejected under 35 U.S.C. 102(b) as being anticipated by Kuntz et al. (1992, The Plant Journal, Vol. 2, No. 1, pages 25-34, Applicant's IDS), for the reasons of record set forth in the office action mailed January 3, 2002.

Applicant's arguments filed April 9, 2002, have been fully considered but they are not persuasive.

Applicant argues that Kuntz et al. fail to disclose an isolated nucleic molecule encoding a prenyltransferase having the nucleic acid sequence of SEQ ID NO:1, and that Kuntz et al. fail to disclose a method for producing a tocopherol compound in a host cell or a method for increasing

the biosynthetic flux in a cell by transforming a host cell with a DNA encoding a prenyltransferase (reply page 10).

While Kuntz et al. fail to disclose an isolated nucleic molecule encoding a prenyltransferase having the nucleic acid sequence of SEQ ID NO:1, the methods of claims 19 and 20 are not limited to isolated nucleic molecules encoding a prenyltransferase having the nucleic acid sequence of SEQ ID NO:1. The methods of claims 19 and 20 are drawn to a nucleic acid sequence encoding a prenyltransferase. Furthermore, claims 19 and 20 do not recite any specific limitations that clearly teach over the prior art of Kuntz et al. The claimed method comprises transforming a prokaryotic or eukaryotic host cell with a construct comprising a nucleic acid sequence encoding a prenyltransferase, operably linked to transcription initiation and termination regions. Kuntz et al. teach transforming a prokaryotic host cell with a construct comprising a nucleic acid sequence encoding a prenyltransferase operably linked to transcription initiation and termination regions. The claims do not elucidate what Applicant did differently from Kuntz et al.

The rejection of claims 1-4, 13-16 and 34 under 35 U.S.C. 102(b) as being anticipated by Zhu et al. (1997, Plant Molecular Biology, Vol. 35, No. 3, pages 331-341, Applicant's IDS) is withdrawn in light of the cancellation of claims 2, 3, 4, 14, 15, 16 and 34, and the amendment of claims 1 and 13.

Claims 19-20 remain rejected under 35 U.S.C. 102(b) as being anticipated by Zhu et al. (1997, Plant Molecular Biology, Vol. 35, No. 3, pages 331-341, Applicant's IDS), for the reasons of record set forth in the office action mailed January 3, 2002.

Applicant's arguments filed April 9, 2002, have been fully considered but they are not persuasive.

Applicant argues that Zhu et al. fail to disclose an isolated nucleic molecule encoding a prenyltransferase having the nucleic acid sequence of SEQ ID NO:1, and that Zhu et al. fail to disclose a method for producing a tocopherol compound in a host cell or a method for increasing the biosynthetic flux in a cell by transforming a host cell with a DNA encoding a prenyltransferase (reply page 11).

While Zhu et al. fail to disclose an isolated nucleic molecule encoding a prenyltransferase having the nucleic acid sequence of SEQ ID NO:1, the methods of claims 19 and 20 are not limited to isolated nucleic molecules encoding a prenyltransferase having the nucleic acid sequence of SEQ ID NO:1. The methods of claims 19 and 20 are drawn to a nucleic acid sequence encoding a prenyltransferase. Furthermore, claims 19 and 20 do not recite any specific limitations that clearly teach over the prior art of Zhu et al. The claimed method comprises transforming a prokaryotic or eukaryotic host cell with a construct comprising a nucleic acid sequence encoding a prenyltransferase, operably linked to transcription initiation and termination regions. Zhu et al. teach transforming a prokaryotic host cell with a construct comprising a nucleic acid sequence encoding a prenyltransferase operably linked to transcription initiation and termination regions. The claims do not elucidate what Applicant did differently from Zhu et al.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

***Remarks***

Claims 19-33, 36, 39 and 42-44 are rejected.

Claims 1, 13 and 18 are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (703) 605-1210. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CC
June 14, 2002

ELIZABETH F. McELWAIN
PRIMARY EXAMINER
GROUP 1600